Non-invasive Interactive Neurostimulation (InterX®) elicits significantly greater physiological response than TENS: Lymphocyte Metabolism and Cytokine production

Introduction:
Non-invasive interactive neurostimulation (InterX) has shown to be clinically effective for a range of acute and chronic conditions. It has been demonstrated that transcutaneous electrical stimulation does not affect the inflammatory response. In a previous study, the effects of InterX or post-treatment were examined. It was demonstrated that lymphocytes post-treatment may be better able to respond to stimuli when necessary, which could result in enhanced healing ability post-injury. The genomic effect on the lymphocytes post-treatment is the result of an acute response that would improve their ability of these cells to respond to injury types of stimuli. We extended this study to include volunteers treated with a TENS device to compare physiological response following a different form of electrical stimulation.

Hypothesis:
This study is hypothesized that significantly greater physiological response will occur following InterX treatment than following TENS. This is suggested in view of the higher amplitude (approximately 5-10 times) and current density (approximately 90 times higher) output of the InterX device.

Method:
Treatment protocol: A multidisciplinary approach was used to examine the effect of transcutaneous interactive neurostimulation using the InterX 5202 device compared to the Biomed 2000XL TENS device on lymphocyte metabolic function and cytokine production. Blood was drawn from healthy adult volunteers prior to and 20 minutes post-treatment. The TENS device had two channels so that the direct area around the elbow, as well as the corresponding nerve root could be treated simultaneously to follow the InterX protocol (Fig.1). The manufacturer recommends to increase the intensity to a level just below that which causes muscle contraction to be followed. 100Hz frequency was used with a pulse width of 150 microseconds. These parameters matched the InterX protocol as closely as possible. Using a higher frequency (200Hz) caused the muscle contraction which may mean using a lower amplitude so in the interests of comparison, frequency was sacrificed in favor of amplitude. The InterX device has small, spaced electrodes which allow for the use of high amplitude stimulation without causing muscle contraction. As TENS electrodes need to be larger and are spaced further apart, muscle contraction occurs at much lower amplitude.

Blood samples were obtained from consented adult volunteers. Non red blood cells (mitochondrial containing cells) were isolated and placed in the chamber of a high resolution respirometry machine (Oroboros, Innsbruck, Austria). All experiments were performed in duplicate. Respiration of the cells in the presence of Glutamate (a favored substrate of lymphocytes) and 2,4-Dinitrophenol (mitochondrial uncoupling for maximum respiration) was recorded. In order to account for differing numbers of cells in the chamber, a BCA protein assay was performed to determine total protein to which the respiration data was normalized.

Results:
The TENS treatment when compared to pre-treatment values, slightly but not significantly increased the maximal respiration in the uncoupled state and there was no discernible difference due to Glutamate and DNP compared with pre-treatment control and compared with InterX.

Conclusion:
This comparative study clearly demonstrates that both TENS and InterX influence similar responses in relation to lymphocyte metabolism and cytokine up regulation. However, the magnitude of that influence is significantly different with InterX having a much greater response in all parameters measured. TENS has a relatively small effect in some cases and a negligible effect in others.

The necessary level of lymphocyte activation needed to elicit a meaningful response to physiological stresses such as injury is unknown, though previous literature has demonstrated that TENS does not have an anti-inflammatory effect. InterX has previously been shown to have an anti-inflammatory effect. The significant differences in the response to the two different types of stimulation may be explained by the fact that InterX delivers a much higher intensity and density of current than TENS as well as delivering stimulation specifically to optimal treatment points.

These data provide only a partial explanation of the inflammatory response and studies relating to circulation and lymphatic flow are warranted to further understand the complex interaction of mechanisms that can elicit a reduction of inflammation in patients. However, this study confirms the hypothesis that InterX elicits significantly greater physiological response than TENS.

References:
8. Einzel, D. L.: Human mast cell stimulation of mast cell release from preformed stores is accompanied by an increase of mitochondrial oxidative events.
17. Glutamate and DNP compared with pre-treatment control and compared with InterX.

Fig 1. InterX and TENS treatment areas

Fig 2. InterX vs TENS. Percentage increase in lymphocyte respiration following activation

Fig 3. InterX vs TENS. Percentage change in lymphocyte cytokine content

IL-1β has been shown to increase mitochondrial oxidative metabolism in pancreatic beta cells, leading to changes in the release of insulin and increased glucose oxidation. IL-6 and TNF-α have both been implicated in liver hypermetabolism, eliciting significantly increased mitochondrial oxidative metabolism. Increased IL-6 levels, both in vitro and in vivo, have been correlated with elevated oxidative stress, increased mitochondrial oxidative stress, and accelerated cell death. Increased IL-6 levels, both in vitro and in vivo, have been correlated with elevated oxidative stress, increased mitochondrial oxidative stress, and accelerated cell death. Increased IL-6 levels, both in vitro and in vivo, have been correlated with elevated oxidative stress, increased mitochondrial oxidative stress, and accelerated cell death. Increased IL-6 levels, both in vitro and in vivo, have been correlated with elevated oxidative stress, increased mitochondrial oxidative stress, and accelerated cell death.